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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,541	03/07/2001	Liselotte Bjerre Knudsen	6169.200-US	4130

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NOVO NORDISK PHARMACEUTICALS, INC
100 COLLEGE ROAD WEST
PRINCETON, NJ 08540

EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/800,541	KNUDSEN, LISELOTTE BJERRE	
	Examiner	Art Unit	
	David S Romeo	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

#A 7/26/4

a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

D.R. 7/26/4

1. ☒ A Notice of Appeal was filed on 6/1/2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

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7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *26-29 and 36-72*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *See Continuation Sheet*

David S Romeo
Primary Examiner
Art Unit: 1647

Continuation of 5. does NOT place the application in condition for allowance because: Claims 26-29, 36-42, 44-46, 48, 49, 51, 52, 54-56, 58, 59, 61, 62, 64-66, 68, 69, 71, 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Eng (a11) in view of Raufman (u11) and in view of Howard (v11).

Claims 26, 27, 29, 36, 37, 39, 40, 42, 43-46, 48, 49, 52-56, 58, 59, 62-66, 68, 69, 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Efendic (b11) in view of Howard (v11).

Applicants argue that the claims require the intent of achieving the purpose given in their respective preambles, and that administering the compounds in the claimed method for some other purpose is not a claimed method. The examiner disagrees with how Applicants' construe the claims. All that the claims require is administering a GLP-1 agonist to a patient in need of lowering of one or more serum lipid levels, reduction of LDL:HDL ratio, or reduction of lipoprotein A. The issue then is whether such a patient knows that he is in need of such lowering or reduction. The examiner has provided evidence that diabetic patients are patients in need of lowering of one or more serum lipid levels, reduction of LDL:HDL ratio, or reduction of lipoprotein A. Specifically, Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction"). Thus, diabetic patients or their care providers know that they are in need of such lowering or reduction. Hence, the claims encompass the treatment of diabetes and the present situation is distinguishable from the decision in Jansen. In the present case the preamble is reduced to the mere statement of an effect which would naturally flow from following the teachings of the prior art. Furthermore, such lowering or reduction is the result of administering a GLP-1 agonist, and the prior art teaches administering GLP-1 agonist to diabetics. Accordingly, the claim is anticipated. In addition, the extra references in the present 35 U.S.C. 102 rejections are use to show that diabetic patients in need of such lowering or reduction. Such a use of multiple references in a 35 U.S.C. 102 rejection is proper.

Claims 26-29, 36-42, 43-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lowering plasma levels of triglycerides, free fatty acids, or total cholesterol, does not reasonably provide enablement for a method of lowering one or more serum lipids, of reducing the serum LDL:HDL ratio, or of reducing the serum level of lp(A) or apo(A).

Applicants argue that the examiner has not provided a reasonable basis for this rejection. Applicant's arguments have been fully considered but they are not persuasive. No changes were observed in the levels of LDL and HDL cholesterol after administration of GLP-1. See Juniti-Berggren (3, cited by Applicants), page 1200, "RESULTS." Neither
Applicants' argument nor the Howard article (cited by Applicants) explain the lack of effect of GLP-1 on the levels of LDL and HDL in the presence or absence of insulin.

Claims 26-29, 36-42, 43-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that the examiner has not provided a reasonable basis for this rejection. Applicant's arguments have been fully considered but they are not persuasive. No changes were observed in the levels of LDL and HDL cholesterol after administration of GLP-1. See Juniti-Berggren (3, cited by Applicants), page 1200, "RESULTS." Neither
Applicants' argument nor the Howard article (cited by Applicants) explain the lack of effect of GLP-1 on the levels of LDL and HDL in the presence or absence of insulin.

Claims 26, 27, 29, 36, 37, 39, 40, 42, 44-49, 52, 54-59, 62, 64-69, 72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that there is a detailed description of analogues, derivatives, and substitutions in the present specification at page 12, line 15, through page 40, line 15. Applicant's arguments have been fully considered but they are not persuasive. The description of analogues, derivatives, and substitutions in the present specification at page 12, line 15, through page 40, line 15, is merely exemplary and does not limit the structure of the analogs and derivatives used in the claimed methods.

Claims 44-49, 52, 54-59, 62, 64-69, 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants argue that there is a detailed description of analogues, derivatives, and substitutions in the present specification at page 12, line 15, through page 40, line 15. Applicant's arguments have been fully considered but they are not persuasive. The description of analogues, derivatives, and substitutions in the present specification at page 12, line 15, through page 40, line 15, is merely exemplary and does not limit the structure of the analogs and derivatives used in the claimed methods.

Claims 26-29, 36-42, 44-50, 52, 54-60, 62, 64-70, 72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39, 40 of U.S. Patent No. 6,268,343 (c11) in view of Howard (v11) and Efendic (b11).

Claims 26-29, 36-42, 44-50, 52, 54-60, 62, 64-70, 72 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20 of U. S. Patent No. 6,458,924 (d11) in view of Howard (v11) and Efendic (b11).

Applicants argue that neither of these patents' claims are directed to the lowering of one or more serum lipids, that the examiner is applying the improper "obvious to try" standard, and that Efendic is distinguished, as above. Applicant's arguments have been fully considered but they are not persuasive. The claims of the patents are directed to the treatment of diabetes or obesity. All that the present claims require is administering a GLP-1 agonist to a patient in need of lowering of one or more serum lipid levels, reduction of LDL:HDL ratio, or reduction of lipoprotein A. The issue then is whether such a patient knows that he is in need of such lowering or reduction. The examiner has provided evidence that diabetic patients are patients in need of lowering of one or more serum lipid levels, reduction of LDL:HDL ratio, or reduction of lipoprotein A. Specifically, Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction"). Thus, diabetic patients or their care providers know that they are in need of such lowering or reduction. In the present case the preamble is reduced to the mere statement of an effect which would naturally flow from following the teachings of the prior art. Furthermore, such lowering or reduction is the result of administering a GLP-1 agonist, and the prior art teaches administering GLP-1 agonist to diabetics or obese, diabetic patients. Hence, the claims encompass the treatment of diabetes or obesity. Application of impermissible "obvious to try" standard usually occurs when invention is made by varying all parameters or trying each of numerous choices until successful without indication in prior art as to which parameters were critical or which choices were likely to be successful, or when invention is made by exploring promising new technology or general approach with only general guidance from prior art as to particular form of claimed invention or how to achieve it. However, in the present case the cited references give specific guidance for the administration of GLP-1 agonists to diabetics or obese, diabetic patients. .

Continuation of 10. Other: Claims 26-29 and 36-72 are subject to a restriction and/or election requirement..